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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/449,817	11/26/1999	Mitchell S. Steiner	P-2762-US1	6736

7590 01/28/2003  
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EXAMINER

KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 01/28/2003

31

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/449,817

Applicant(s)

STEINER ET AL.

Examiner

Kathleen M Kerr

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 12 November 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1,7,10-27,30-36,40,44,45,47 and 54-60 is/are pending in the application.
- 4a) Of the above claim(s) 30-36,40,44,45,47 and 58 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,7,10-27,54-57,59 and 60 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 30.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Application Status***

1. In response to the previous Office action, a first Office action on the merits (Paper No. 27, mailed on March 25, 2002), Applicants filed an amendment and response received on September 26, 2002 (Paper No. 28). Said amendment amended Claims 1, 7, 10-12, 17-21, 23, 54-57, 59, and 60. Claims 1, 7, 10-27, 30-36, 40, 44, 45, 47, and 54-60 are pending in the instant Office action.

### ***Election***

2. This application contains Claims 30-36, 40, 44, 45, 47, and 58 drawn to an invention nonelected with traverse in Paper No. 26. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 C.F.R. § 1.144) See M.P.E.P. § 821.01.

Claims 1, 7, 10-27, 30-36, 40, 44, 45, 47, and 54-60 are pending in the instant application. Claims 30-36, 40, 44, 45, 47, and 58 remain withdrawn from consideration as nonelected inventions. Thus, Claims 1, 7, 10-27, 54-57, 59, and 60 will be examined herein.

### ***Priority***

3. As previously noted, the instant application is granted the benefit of priority for the U.S. non-Provisional Application No. 09/302,457 filed on April 29, 1999 while the elected subject matter has priority back to only the filing date of the instant application that is November 26, 1999.

***Information Disclosure Statement***

4. The information disclosure statement filed on November 12, 2002 (Paper No. 30) has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy. The Examiner notes that numerous citation errors have been corrected by the Examiner; no action is required by Applicants.

***Drawings***

5. The drawings are considered informal for the reasons detailed in the copy of PTO Form 948 attached to Paper No. 27. Appropriate correction is required in response to the instant Office action and may not be held in abeyance (see 37 C.F.R. § 1.85(a)).

***Compliance with the Sequence Rules***

6. In response to the previous Office action requiring a statement of sameness and no new matter for the paper copy and computer readable form copy of the sequence listing on August 16, 2001 (Paper No. 21), Applicants filed a statement under 37 C.F.R. § 1.821(f). However, this statement is insufficient since it notes that the sequence listing is "forwarded herewith". Such a statement must refer to the sequence listing filed on April 16, 2001 to render the instant application in full compliance with the sequence rules. A new statement of sameness and no new matter is required.

***Withdrawn - Objections to the Specification***

7. Previous objection to the specification for improperly incorporating required materials by reference is withdrawn by virtue of Applicant's amendment introducing the description of the

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construction of AdRSVpHyde, which has previously been incorporated from the parent application 09/302,457.

8. Previous objection to the title is withdrawn by virtue of Applicants' amendment.

***Maintained – Objections to the Specification***

9. Previous objection to the specification for containing confusing reference materials is maintained. Applicants have not commented on the previous objection, which is repeated herein for completeness.

“Throughout the application, for example on page 25, line 25, bracketed references such as “[74]” are found but do not correlate to the reference citations at the end of the application. Amendment to these references must be added to include the proper citations. Also, “?” are found throughout the specification, for example on page 77, line 32. Their meaning is unclear and should be amended into the specification. Applicants must cite page and line number from the instant application or any incorporated references to identify clear support as originally filed for any amendment.”

10. Previous objection to the Abstract is maintained. Applicants have amended the abstract, but said amendment has not completely obviated the previous objection. As previously noted, the Abstract is objected to for not completely describing the disclosed subject matter. The Examiner suggests the inclusion of the function of p-Hyde protein as well as both source species, human **and rat**, for completeness. Applicants are reminded that the Abstract must describe the entire disclosure and not just what is claimed. Correction is required.

***Withdrawn - Claim Objections***

11. Previous objection to Claims 1, 7, 10-11, 16-27, 54-57 and 59-60 for containing non-elected subject matter is withdrawn by virtue of Applicants' amendment removing reference to sequences other than SEQ ID NOs:1 and 2.

***Withdrawn - Claim Rejections - 35 U.S.C. § 112, second paragraph***

12. Previous rejection of Claims 1, 7, 10-27, 54-57, and 59-60 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "isolated nucleic acid" is withdrawn by virtue of Applicants' amendment.

13. Previous rejection of Claims 12-15 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "which encodes **the** human p-Hyde of claim 1" (emphasis added) is withdrawn by virtue of Applicants' amendment.

14. Previous rejection of Claim 19 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "operatively, or an expression element linked to the nucleic acid" is withdrawn by virtue of Applicants' amendment.

15. Previous rejection of Claims 23-24 under 35 U.S.C. § 112, second paragraph, as being indefinite for the composition of the adenovirus vector, as found in Claim 23, is withdrawn by virtue of Applicants' amendment.

16. Previous rejection of Claims 54-56 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "similarity" is withdrawn by virtue of Applicants' amendment removing

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the term. A new rejection is set forth below, however, for the term “complementary” as used in the instant claims.

***Maintained - Claim Rejections - 35 U.S.C. § 112, second paragraph***

17. Previous rejection of Claims 1, 7, 10-27, 54-57, and 59-60 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term “analog” is maintained. Applicants’ arguments have been fully considered but are not deemed persuasive. Applicants argue that the term “analog” is clear to a person of skill in the art; however, Applicants provide no definition to be used. The Examiner maintains the term to be unclear. For example, must the activity be retained by an “analog”? Is so, what activity is that? Must the structure be retained by an “analog”? If so, how much structure? Applicants have provided no answers to the above questions, previously presented, to help clarify the metes and bounds of the term “analog”. Applicants also argue that an “analog” must encode a p-hyde protein as defined in the specification. However, the specification is wholly unclear as to what a p-hyde protein is other than particularly SEQ ID NO:2 in human. For all of the above reasons, the instant rejection is maintained.

18. Previous rejection of Claim 16 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase “sequence complementary to” is maintained. Applicants present no arguments in traverse. As previously noted, Claim 1 encompasses DNA, which is double stranded, already containing a “complementary” sequence to the gene that encodes the protein. Which sequence must it be complementary too?

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19. Previous rejection of Claims 21-24 under 35 U.S.C. § 112, second paragraph, as being indefinite for the abbreviation “BAC” is maintained. Applicants’ arguments have been fully considered but are not deemed persuasive. Applicants argue that the amendment filed obviated the rejection; this is not the case for “BAC”. The Examiner suggests that “BAC artificial chromosome” be replaced by ---bacteria artificial chromosome (BAC)--- for clarity.

***Maintained - Claim Rejections - 35 U.S.C. § 112, first paragraph***

20. Previous rejection of Claims 1, 7, 10-27, 54-56 and 59 under 35 U.S.C. § 112, first paragraph, written description, is maintained. Applicants’ arguments have been fully considered but are not deemed persuasive for the following reasons. Applicants argue that the instant claims are definite; however, the instant rejection is a rejection of description, i.e., how adequately the specification describes the claimed genus. Thus, such arguments are not persuasive. It is maintained that the instant claims required both structural and functional limitations to support the claimed genus. A portion of the previous rejection is repeated below for completeness:

“The instant specification discloses cDNA sequences from human (SEQ ID NO:1) and rat (SEQ ID NO:3) encoding a “p-Hyde” protein. This p-Hyde protein is disclosed as having the ability to induce cell-death-susceptibility in a cancer cell; this activity is tested using only the rat protein, which is 489 amino acids long; the deduced human protein is 186 amino acids long.

The specification adequately describes the two species of human and rat cDNA sequences encoding p-Hyde. The specification also adequately describes the genus of p-Hyde cDNAs whose structure and function are clearly related to the disclosed sequences, i.e., being at least 90% identical to SEQ ID NO:1 and encoding a protein having the ability to induce cell-death-susceptibility in a cancer cell. However, the structures of “analogs, fragments, variants, and mutants” and the structure of the “genomic” DNA related to the disclosed species cannot be reasonably predicted by one of skill in the art using only the disclosed species as guides. No structural analysis of the p-Hyde cDNA is disclosed to indicate functional domains or the like. No information about introns can be predicted from the cDNA. Thus, when varying the disclosed sequence, one of skill in the art could not reasonably predict which portion of the sequences retain which homologies so that the claimed activity would be retained.”



***Maintained - Claim Rejections - 35 U.S.C. § 101***

21. Previous rejection of Claims 1, 7, 10-27, 54-57, and 59-60 under 35 U.S.C. § 101 because the claimed invention lacks patentable utility is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. Applicants argue that the subject matter of the instant claims is "functionally and structurally characterized in the subject Application" through experiments. The Examiner disagrees. As previously noted, the rat p-Hyde protein has been characterized. The instant claims are drawn to the human p-Hyde protein that is highly dissimilar from the rat without any evidence to indicate that the same structure/function applies to the human sequence. For these reasons, the instant rejection is maintained. A portion of the previous rejection is repeated below for completeness:

"The instant claims are drawn to a nucleic acid sequence (p-Hyde gene) encoding a human p-Hyde protein. A p-Hyde protein from rat is characterized in the instant specification; the experiments presented for the rat protein indicate that rat p-Hyde has the ability to induce cell-death-susceptibility in a cancer cell. It can be reasonably assumed that other p-Hyde proteins from other mammals will possess the same, or closely related, activity. The utility of the claimed invention relies on the activity proposed for the rat protein.

The utility of the rat protein and gene cannot be translated into utility for the human protein and gene because it is unclear that the sequences are related. The instant specification discloses cDNA sequences from human (SEQ ID NO:1) and rat (SEQ ID NO:3) encoding a "p-Hyde" protein. These DNA sequences share a region of 84% identity (see attached alignment). The rat protein is 489 amino acids long from a cDNA open reading frame of 1467 base pairs. The human protein is 186 amino acids long from a cDNA open reading frame of 637 base pairs (disclosed SEQ ID NO:1 also contains non-coding regions from 1-78 and from 638-733). It is not convincing that a rat protein of 489 amino acids would have a homolog in human of 186 amino acids, especially one so dissimilar in sequence. Moreover, no structural, domain analysis of the rat sequence has been offered to demonstrate a functional domain that is retained in the shorter human sequence. Thus, without convincing evidence that the disclosed human sequence actually encodes a p-Hyde homolog, the claimed nucleic acid sequences lack a patentable utility.

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22. Previous rejection of Claims 1, 7, 10-27, and 54-60 under 35 U.S.C. § 112, first paragraph, enablement, is also maintained for the reasons noted above in the maintaining of the utility rejection.

***Maintained - Claim Rejections - 35 U.S.C. § 102***

23. Previous rejection of Claims 1, 7, 12, 13, 16, 17 under 35 U.S.C. § 102(b) as being anticipated by Hillier *et al.* is maintained. Applicants' arguments have been fully considered but are not deemed persuasive. Applicants argue that the mRNA sequence of Hillier *et al.* is not SEQ ID NO:1. However, such metes and bounds are only pertinent to Claim 57, which is not rejected over Hillier *et al.* A portion of the previous rejection is repeated below for completeness.

“Hillier *et al.* teach a human mRNA EST sequence that matches 155 nucleotides of Applicants' SEQ ID NO:1 (see attached alignment). Said EST will specifically hybridize with SEQ ID NO:1 and teaches the complementary or antisense sequences due to the inherent complementarity of DNA molecules.”

24. Previous rejection of Claims 1, 7, 10-21, 25-27, 54-56 and 59 under 35 U.S.C. § 102(b) as being anticipated by Talerman *et al.* is maintained. Applicants' arguments have been fully considered but are not deemed persuasive. Applicants argue that the DNA sequence of Talerman *et al.* is not SEQ ID NO:1. However, such metes and bounds are only pertinent to Claim 57, which is not rejected over Talerman *et al.* A portion of the previous rejection is repeated below for completeness.

“Talerman *et al.* teach a DNA sequence that is 72% similar and 39% identical to Applicants' SEQ ID NO:1 (see attached alignment). Talerman *et al.* also teach fluorescent labels on their DNA, hybridization techniques, and techniques using promoters, BAC vectors, and stably transfected murine host cells (see pages 15-16).”

***Reiterated - Examiner's Comment***

25. For clarity of the record, the Examiner requests an explanation for the omission of Chiang Wang as an inventor of the claimed invention. Chiang Wang appears, with the other inventors, as an inventor in the WIPO document, WO 2000 071564 A2. Comment concerning the inventorship of the instant application, with respect to Chiang Wang, is required in response to the instant Office action.

26. As previously noted, the Examiner suggests the inclusion of the 489 amino acid rat protein deduced from the 1467 base pair cDNA in the sequence listing. The Examiner previously suggested such an inclusion; Applicants neither added the sequence nor commented on why it was not necessary. As previously noted, often times, a disclosed protein can be overlooked because only its encoding DNA sequence is searchable (in a sequence listing). For completeness, the inclusion of the rat protein sequence is recommended. The rat full-length protein sequence would not be considered new matter if it is *exactly* encoded by the cDNA disclosed in SEQ ID NO:3. An alignment of the coding DNA and the added amino acid should be included to clearly show support and the lack of new matter.

**NEW OBJECTIONS/REJECTIONS**

***Claim Objections***

27. Claim 7 is objected to for having an improper Markush group. The members of a Markush group must be independent and non-overlapping. In Claim 7, the group "c-DNA" is included in the group "DNA"; thus, the Markush group is improper. Correction is required.

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28. Claims 12-17 are objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 12-17 are drawn to complementary or antisense sequences, none of which are encompassed by Claim 1, as amended.

29. Claim 14 is objected to for having an improper format and for being inconsistent with previous claims. A period is required at the end of the claim. Also, the claim should depend from Claim 14 and cite ---wherein the detectable marker--- and not “wherein the oligonucleotide” for consistency with previous claims. Correction is required.

30. Claim 59 is objected to for depending from a non-elected claim, Claim 53. This appears to be a typographical error since Claim 59 previously depended from 54 (considering misnumbering issues). Claim 59 will be examined as if it depends from Claim 54. Appropriate correction is required.

***Claim Rejections - 35 U.S.C. § 112***

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

31. Claims 54-56 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase “having at least 75% complementary to” is wholly confusing. The Examiner suggests the term ---identity--- for clarity.

***Summary of Pending Issues***

32. The following is a summary of the issues pending in the instant application:

- a) Non-elected Claims 30-36, 40, 44, 45, 47, and 58 remain pending and must be cancelled in response to this Final office action.
- b) The drawings are considered informal.
- c) The instant application is not in full compliance with the sequence rules.
- d) The specification stands objected to for containing confusing reference materials.
- e) The Abstract stands objected to for being incomplete.
- f) Claim 7 stands objected to for having an improper Markush group.
- g) Claims 12-17 stand objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.
- h) Claim 14 stands objected to for having an improper format and for being inconsistent with previous claims.
- i) Claim 59 stands objected to for depending from a non-elected claim, Claim 53.
- j) Claims 1, 7, 10-27, 54-57, and 59-60 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "analogs".
- k) Claim 16 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "sequence complementary to".
- l) Claims 21-24 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the abbreviation "BAC".
- m) Claims 54-56 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "having at least 75% complementary to".
- n) Claims 1, 7, 10-27, 54-56 and 59 stand rejected under 35 U.S.C. § 112, first paragraph, written description.
- o) Claims 1, 7, 10-27, and 54-60 stand rejected under 35 U.S.C. § 112, first paragraph, enablement.
- p) Claims 1, 7, 10-27, 54-57, and 59-60 stand rejected under 35 U.S.C. § 101.
- q) Claims 1, 7, 12, 13, 16, 17 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Hillier *et al.*
- r) Claims 1, 7, 10-21, 25-27, 54-56 and 59 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Talerman *et al.*
- s) A question of inventorship must be addressed.

All the above issues must be addressed in response to the instant Office action for said response to be considered fully responsive.

***Conclusion***

33. Claims 1, 7, 10-27, 54-57, and 59-60 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



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KMK

January 25, 2003